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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/717,559
Filing Date: November 21, 2003
Appellant(s): LIN ET AL.

Richard E. Fichter
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed August 25, 2008 appealing from the Office action mailed December 10, 2007.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct. However, the status of claims does not mention that there has been an election of species in this case. In response to the election of species requirement of March 22, 2007, the appellant elected a specific lanostane compound of formula (I) where R_2 is $OCOCH_3$. The claims have been examined solely in regards to this elected species.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

NEW GROUND(S) OF REJECTION

Claims 6-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

WITHDRAWN REJECTIONS

The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner. The rejection of claim 6-13 under 35 U.S.C. 103(a) as being unpatentable over Babish et al. (US 2002/0068098) in view of Cuellar et al. (Chemical and Pharmaceutical Bulletin (1997), vol. 45, no, 3, pp. 492-494) and Tai et al. (Phytochemistry (1995), vol. 39, no. 5, pp. 1165-1169) has been withdrawn.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Takahashi et al. Japanese Patent Application Number 8-119864 (May 1996). Full English translation.

Tai et al. Phytochemistry (1995), vol. 39, no. 5, pp. 1165-1169.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 6-13 stand finally rejected under 35 U.S.C. 103(a) as being unpatentable over Takahashi et al. (JP 8-119864) in view of Tai et al. (Phytochemistry. 1995. Vol. 39, No. 5. pp. 1165-1169).

Note a full translation of the Japanese Patent will be used for citation purposes and previously has been provided to the appellant.

Takahashi et al. teach the compound of formula 13 and formula 14, which reads on the elected species in instant claim 6 where R_2 is CH_3COO (paragraph [0007]). The compound of formula 13 is 10% by weight of a 200 mg tablet (paragraph [0049]). The compound of formula 13 is administered orally to humans (paragraph [0036]).

Takahashi et al. further teach the extraction of the compound of formula 13 and the compound of formula 14, which reads on the elected species in instant claim 6 where R_2 is CH_3COO (paragraph [0011]). Poria sclerotium is extracted with methanol and the extract contains 0.7% lanostane compounds of formula (I) relative to the initial amount of Poria extract (paragraph [0011]). The resulting liquid extract was concentrated with reduced pressure, subjected to silica gel column chromatography, and eluted with chloroform and methanol (50:1) to create four fractions (paragraph [0011]). Table 1 shows that further fractionation of Fraction B leads to a product that contains polyporenic acid, pachymic acid, and dehydropachymic acid. These three compounds are all defined by the reference as lanostane compounds (see paragraph [0007], [Chem. 11], [Chem. 12], [Chem 13], and [Chem. 14]). Table 1 does not identify the

detection of any secolanostane compounds in this fraction. Thus, this fraction is considered to be "substantially devoid" of secolanostane compounds.

Takahashi et al. do not teach the step of concentrating the eluate to form a concentrated eluate with thin layer chromatography (TLC) in the extraction of *Poria cocos*.

Tai et al. teach extraction of various lanostane compounds of formula (I) (page 1168). The extraction involves exposing the sclerotia of *Poria cocos* to methanol (page 1168). The liquid extract was dried and concentrated with Et_2O (pages 1168-1169). The resultant concentrated extract was introduced into a silica gel column with $CHCl_3$ and MeOH-$CHCl_3$ gradient mixtures (page 1169). The extract was rechromatographed on a silica gel column with MeOH-$CHCl_3$ (page 1169). Purification was performed using TLC with MeOH-$CHCl_3$ (1:199) (page 1169).

To a person of skill in the art at the time of the invention, it would have been obvious to employ the purification with TLC taught by Tai et al. in the method of extraction of lanostanes taught by Takahashi et al. because Tai et al. demonstrates that it was known in the art at the time of the appellant's invention that TLC is suitable for use in purifying lanostanes. Since both references are concerned with the same problem, specifically the purification of lanostanes, an artisan of ordinary skill would have reasonably expect that the lanostane extraction taught by Takahashi could produce a further purified product if a TLC step such as that taught by Tai et al. was added to the extraction procedure. This reasonable expectation of successful results would have motivated the artisan to modify the extraction procedure taught by Takahashi to include the TLC purification steps taught by Tai et al.

Regarding 5-60% and 10-20% of the lanostane (I) as recited in instant claims 6 and 12, Takahashi et al. teach *Poria cocos* extracts containing about 0.7% by weight of lanostane (I) compounds in regards to the initial weight of Poria extract (paragraph [0011]). It is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the weight of the lanostane (I) compounds provided in a composition, according to the guidance set forth in Takahashi et al., to provide an extract having the desired percentage weight of the lanostane (I) compounds in *Poria cocos* extracts. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 223, 235 (CCPA 1955).

Regarding the chromatographic value, Rf, and the mixed solvent as recited in instant claim 8, it would be obvious to one skilled in the art at the time of the invention to change the solvent used and thus change the Rf value in order to meet the limitations of the claim. Solvents are routinely changed due to the polarity of the compounds to extract and the availability of the solvent. Because the solvents can be changed, the resulting Rf will also change.

Regarding 95% ethanol as recited in instant claim 9, Takahashi et al. teach extraction of lanostane (I) compounds with ethanol (paragraph [0011]) and Tai et al. teach extraction of lanostane (I) compounds with methanol (page 1168), which meets the limitations of the instant claims. It is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the percentage of methanol provided in a composition, according to the guidance set forth in Takahashi et al. and Tai et al., to provide a composition having the desired percentage of methanol. It is noted that "[W]here the general

conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 223, 235 (CCPA 1955).

Regarding the two-phase solvent as recited in instant claim 10 and the mixed solvent as recited in instant claim 11, it would be obvious to one skilled in the art at the time of the invention to change the solvent used in order to meet the limitations of the claims. Solvents are routinely changed due to the polarity of the compounds to extract and the availability of the solvent.

NEW GROUND(S) OF REJECTION

Claims 6-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "substantially" in claim 6, line 3, is a relative term which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Claim 6 states that the Poria extract must be "substantially devoid of secolanostane." The specification does not provide any definition or guidelines that could be used to determine what amounts of secolanostane could be present in the extract and still have the extract be considered "substantially devoid of secolanostane." Thus, an artisan of ordinary skill could not reasonably ascertain the metes and bounds of the claims. Claim 7-13 are indefinite in that they depend from claim 6 and do not clarify this 112 2nd paragraph issue.

The term "low" in reference to the eluent polarity in claim 7, step d), is a relative term which renders the claim indefinite. The term "low" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Regarding the "low" polarity eluent, page 7, lines 11 and 12 of the specification state "It is recommended that the low polarity eluent is a mixed solvent containing dichloromethane and methanol…". The use of "It is recommended" in the definition of a low polarity eluent does not provide a closed definition for "low polarity." Thus, the specification does not provide a limiting definition for eluents that are considered to be "low polarity." Therefore, an artisan of ordinary skill could not reasonably ascertain what eluents are encompassed by this limitation. Accordingly, the metes and bounds of the claim are unclear. Claims 8-10 are indefinite in that they depend from claim 7 and do not clarify this issue.

(10) Response to Argument

Regarding the 103 rejection based on the combination of Takahashi and Tai, the appellant argues that the claimed invention is patentable because the appellant has discovered that a low polarity extract of Poria is capable of enhancing the immunity of the human body and is devoid of inhibitive components such as secolanostanes and higher polarity molecules contained in the high polarity portion. The appellant also argues that the limitation in the preamble that the claimed extract is capable of "enhancing immunity" should be given patentable weight because it differentiates the claimed extract from the prior art extracts.

However, these arguments are not persuasive. Takahashi produces a Poria extract using an extraction procedure that is substantially identical to the extraction procedure claimed by the appellant in claim 7. The reference teaches extraction of hoelen in paragraph [0011]. "Hoelen" is defined by the reference as being a portion of the sclerotium of *Poria cocos* (paragraph [0003]). The hoelen is extracted with methanol (paragraph [0011]). This corresponds to step a) in appellant's claim 7. The extraction solution is concentrated by filtration and then removal of the solvent (see paragraph [0011]). This corresponds to step b) in appellant's claim 7. The concentrated extract is then subjected to silica gel column chromatography (see paragraph [0011]). This corresponds to step c) in appellant's claim 7. The extract is then eluted with chloroform and methanol to obtain four fractions, termed Fractions A-D (see paragraph [0011]). The reference does not specifically define this eluent as a "low polarity" eluent. However, appellant's claim 8 states that the low polarity eluent contains methanol. The eluent used in the reference also contains methanol. Therefore, an artisan of ordinary skill would reasonably conclude that the eluent used in the reference is a low polarity eluent due to the fact that both the reference and the claims share the use of methanol as the eluent. Thus, the reference also teaches a step that corresponds to step d) in appellant's claim 7. Table 1 in the reference shows that fraction B is further concentrated using solvent fractionation. This corresponds to step e) in appellant's claim 7. Table 1 in the reference examines the resulting fraction and shows that this fraction contains polyporenic acid, pachymic acid, and dehydropachymic acid all of which are lanostane compounds (see paragraph [0007], [Chem. 11], [Chem. 12], [Chem 13], and [Chem. 14]). This fraction is not reported as containing secolanostane compounds. Table 1 shows that the secolanostane compounds are found in fraction D. Thus, the fraction reported as containing

polyporenic acid, pachymic acid, and dehydropachymic acid was examined for secolanostanes and does not contain these compounds. Therefore, this fraction meets the appellant's limitation that the extract composition is "substantially devoid" of secolanostane compounds. The reference does not give the weight of this fraction; thus, it is unclear what percentage of lanostane compounds are present in this fraction. However, since the extraction procedure taught by the reference is substantially identical to the extraction procedure taught by the appellant, it is reasonable to assume that the concentration of the lanostane compounds in the reference extract are at least overlapping, if not identical, to the percentages claimed by the appellant. Therefore, since the extract taught by the reference reasonably appears to be identical to the extract claimed by the appellant, the reference extract would intrinsically have the same pharmaceutical properties as the claimed extract. Thus, the reference extract would have the same ability to "enhance immunity" as the claimed extract. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

The appellant argues that the Final Rejection does not properly set forth a case for obviousness because a conclusion that the claimed invention is obvious because all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness. The appellant further argues that the conclusion of obviousness set forth in the Final Rejection is based on conclusory statements rather than articulated reasoning. The appellant argues that there is no motivation to combine Tai and Takahashi to arrive at the presently claimed invention. However, the Final Rejection contained clear reasoning for the

determination of obviousness. This reasoning is reproduced above. In addition, both references are concerned with the same problem, specifically the purification of lanostanes. Combining known methods for solving the same problem is considered to be *prima facie* obvious. An artisan of ordinary skill would have reasonably expected that the lanostane extraction taught by Takahashi could produce a further purified product if a TLC step such as that taught by Tai was added to the extraction procedure. This reasonable expectation of successful results would have motivated the artisan to modify the extraction procedure taught by Takahashi to include the TLC purification steps taught by Tai.

The appellant also argues that the Poria extract created in the reference contains 0.12% of secolanostane as shown in Fraction D of Table 1. The appellant argues that this "high content of secolanostane in the extract" is contrary to the teaching of the current invention to limit the amounts of secolanostane. The appellant argues that there is no motivation to remove the secolanostanes from the reference extract. However, as discussed above, Fraction D is only one of four extracts created from the initial crude Poria extract. Fraction D shows that there is 0.12% of secolanostanes in the initial extract of Poria. The appellant has not recognized that the reference teaches three additional fractions from Poria and that the reference analyzes a fraction from Fraction B and does not detect *any* secolanostanes in this fraction. Thus, the product from Fraction B meets the appellant's limitation that the product is "substantially devoid" of secolanostanes. Furthermore, since the appellant has not defined the metes and bounds of "substantially devoid," it is unclear if an amount of 0.12% of secolanstanes would be excluded from the claimed extract. An artisan would reasonably conclude that such as small amount would fall within "substantially devoid."

The appellant also argues that there is a lack of motivation to prepare a Poria extract that comprises 5 to 60% of a lanostane by weight because the reference teaches that secolanostanes are also active in the treatment taught by the reference. However, the reference does analyze each of the active component individually and shows that the lanostane, polyporenic acid C is the most effective of the compounds. Thus, an artisan would have been motivated to use this compound and extracts containing this compound because the artisan would have expected that this would produce the most effective pharmaceutical. This would provide motivation for the artisan to modify the extraction procedure to optimize the amount of polyporenic acid C in the Poria extract. In addition, as discussed above, the extraction procedure taught by the reference to arrive at the fraction product from Fraction B is substantially identical to the extraction procedure taught by the appellant. Thus, it is reasonable to assume that the concentration of the lanostane compounds in the reference Fraction B extract product are at least overlapping, if not identical, to the percentages claimed by the appellant.

The appellant argues that the examiner has ignored "the limitation of claim 7 which specifies e) concentrating the eluate to form a concentrated eluate, wherein the concentrated eluate from step e) has a chromatographic value, Rf, not less than 0.1 in accordance with a thin layer chromatography, which is developed by a mixed solvent of dichloromethane : methanol = 96:4 and is detected by an ultraviolet lamp and iodine vapour" (page 10 of the Appeal Brief). It must be noted that the limitations "wherein the concentrated eluate from step e) has a chromatographic value, Rf, not less than 0.1 in accordance with a thin layer chromatography, which is developed by a mixed solvent of dichloromethane : methanol = 96:4 and is detected by an ultraviolet lamp and iodine vapour" are found in claim 8 not in claim 7. As discussed above,

Takahashi teaches an extraction procedure that is substantially identical to the extraction procedure set forth in claim 7. In regards to the limitations set forth in claim 8, Tai provides motivation for using TLC to purify the compounds taught in Takahashi because Tai shows that this was a known method for purification of lanostane compounds. Tai does not specifically teach dichloromethane and methanol to develop the fractions. However, as discussed above, solvents are routinely changed due to the polarity of the compounds to extract and the availability of the solvent. Because the solvents can be changed, the resulting Rf will also change. Furthermore, claim 8 is drawn to a product-by-process claim. The appellant has not provided any concrete evidence to support the assertion that the product produced by the combination of Takahashi and Tai would contain secolanostanes. The evidence on the record supports a conclusion that the extract taught by Takahashi is the same as the claimed extract based on the substantial similarity between the extraction procedures and the analysis of Fraction B shown in Table 1 of Takahashi.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

This examiner's answer contains a new ground of rejection set forth in section **(9)** above. Accordingly, appellant must within **TWO MONTHS** from the date of this answer exercise one

of the following two options to avoid *sua sponte* **dismissal of the appeal** as to the claims subject to the new ground of rejection:

(1) **Reopen prosecution.** Request that prosecution be reopened before the primary examiner by filing a reply under 37 CFR 1.111 with or without amendment, affidavit or other evidence. Any amendment, affidavit or other evidence must be relevant to the new grounds of rejection. A request that complies with 37 CFR 41.39(b)(1) will be entered and considered. Any request that prosecution be reopened will be treated as a request to withdraw the appeal.

(2) **Maintain appeal.** Request that the appeal be maintained by filing a reply brief as set forth in 37 CFR 41.41. Such a reply brief must address each new ground of rejection as set forth in 37 CFR 41.37(c)(1)(vii) and should be in compliance with the other requirements of 37 CFR 41.37(c). If a reply brief filed pursuant to 37 CFR 41.39(b)(2) is accompanied by any amendment, affidavit or other evidence, it shall be treated as a request that prosecution be reopened before the primary examiner under 37 CFR 41.39(b)(1).

Extensions of time under 37 CFR 1.136(a) are not applicable to the TWO MONTH time period set forth above. See 37 CFR 1.136(b) for extensions of time to reply for patent applications and 37 CFR 1.550(c) for extensions of time to reply for ex parte reexamination proceedings.

Respectfully submitted,

/Susan Coe Hoffman/
Primary Examiner, Art Unit 1655

A Technology Center Director or designee must personally approve the new ground(s) of rejection set forth in section (9) above by signing below:

/Remy Yucel/

Director, Technology Center 1600

Conferees:

/Terry A. McKelvey/

Supervisory Patent Examiner, Art Unit 1655

/Cecilia Tsang/

Supervisory Patent Examiner, Art Unit 1654